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<p>Substitute for Form 1449/A/PTO</p> <p><b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> (use as many sheets as necessary)</p> <p>SEP 14 2005 U.S. PATENT &amp; TRADEMARK OFFICE</p>				Complete if Known	
				Application No.	09/644,387
				Filing Date	08/23/2000
				First Named Inventor	Agoston et al.
				Group Art Unit	1617
				Examiner Name	Barrio, Barbara
Sheet	1	of	24	Attorney Docket Number	05213-0541 (43170-219662)

**U.S. PATENT DOCUMENTS**

Examiner Initials	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)			
BB	1	3,166,577		Ringold et al.	01/19/1965	
	2	3,562,260		De Ruggieri et al.	02/09/1971	
	3	4,444,767		Torelli et al.	04/24/1984	
	4	4,552,758		Murphy et al.	11/12/1985	
	5	4,634,705		DeBernardis et al.	01/06/1987	
	6	4,808,402		Leibovich et al.	02/28/1989	
	7	5,629,327		D'Amato	05/13/1997	
	8	5,629,340		Kuwano et al.	05/13/1997	
	9	5,639,725		O'Reilly et al.	06/17/1997	
	10	5,646,136	A	Petrow	07/08/1997	
	11	5,716,981		Hunter et al.	02/10/1998	
	12	5,733,876		O'Reilly et al.	03/31/1998	
	13	5,763,432		Tanabe et al.	06/09/1998	
	14	5,776,704		O'Reilly et al.	07/07/1998	
	15	5,792,845		O'Reilly et al.	08/11/1998	
	16	5,837,682		O'Reilly	11/17/1998	
	17	5,854,205		O'Reilly et al.	12/29/1998	
	18	5,854,221		Cao et al.	12/29/1998	
	19	5,861,372		Folkman et al.	01/19/1999	
	20	5,885,795		O'Reilly et al.	03/23/1999	
	21	5,919,459	A	Nacy et al.	07/06/1999	
	22	5,958,892		Mukhopadhyay et al.	09/28/1999	
	23	6,011,023		Clark et al.	01/04/2000	
BB	24	6,046,186		Tanabe et al.	04/04/2000	

Examiner Signature	<i>Barrio</i>	Date Considered	<i>11/15/05</i>
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<sup>1</sup>Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language translation is attached.

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Sheet	2	of	24	Attorney Docket Number	05213-0541 (43170-219662)

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		Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)			
BB	25	6,051,726	A	Sachdeva et al.	04/18/2000	
	26	6,054,598		Sachdeva et al.	04/25/2000	
	27	6,239,123		Green et al.	05/29/2001	
	28	6,284,789	BI	LaLonde et al.	09/04/2001	
	29	6,346,510	BI	O'Reilly et al.	02/12/2002	
	30	6,399,773	BI	Liu et al.	06/04/2002	
	31	6,410,029	BI	Mukhopadhyay et al.	06/25/2002	
	32	6,413,513	BI	Holaday, John	07/02/2002	
	33	6,514,971	BI	Thomas et al.	02/04/2003	
	34	6,528,676	BI	D'Amato et al.	03/04/2003	
	35	6,605,622	B2	Green et al.	08/12/2003	
	36	6,723,858	B2	D'Amato et al.	04/20/2004	
	37	6,730,665	BI	Maran et al.	05/04/2004	
	38	6,908,910	B2	D'Amato et al.	06/21/2005	
	39	2002/0002294	A1	D'Amato et al.	01/03/2002	
	40	2002/0165212	A1	D'Amato et al.	11/07/2002	
	41	2003/0027803	A1	Slaga et al.	02/06/2003	
	42	2003/0096800	A1	D'Amato et al.	05/22/2003	
	43	2003/0236408	A1	D'Amato et al.	12/25/2003	
	44	2004/0072813	A1	D'Amato et al.	04/15/2004	
	45	2004/0214807	A1	D'Amato et al.	10/28/2004	
BB	46	2005/0020555	A1	D'Amato et al.	01/27/2005	

Examiner Signature	Badio	Date Considered	11/15/05
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<sup>1</sup>Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. \*Applicant is to place a check mark here if English language translation is attached.

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					Group Art Unit	1617
					Examiner Name	Badio, Barbara
Sheet	3	of	24		Attorney Docket Number	05213-0541 (43170-219662)

**FOREIGN PATENT DOCUMENTS**

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		Office <sup>2</sup>	Number <sup>3</sup> (if known)				
	47	DE	2 004 516	VEB Jenapharm	09/10/1970		No
			English translation attached				
	48	DE	27 57 157	Schering AG	12/19/1977		
			English translation not attached				
BB	49	EP	0657175	A2	Centro de Immunologia Molecular	06/14/1995	
	50	EPO	0166937	A2	Abbott Laboratories	08/01/1986	
	51	GB	857,080		Syntex S.A.	12/29/1960	
	52	GB	857,081		Syntex S.A.	12/29/1960	
	53	GB	1,570,597		Takeda et al.	07/02/1980	
	54	JP	42-928	B	DAINIPPON PHARM CO LTD (abstract only)	01/18/1967	
	55	JP	39-5480	B	Teikoku Hormone Mfg. Co.		No
	56	JP	09316000	A	Toagosei Co. Ltd. (English Abstract only)	09/12/1997	
	57	JP	58-131978		Lilly & Co Eli (Eli) (English Abstract only)	08/06/1983	No
	58	JP	63090763	A	Research Development Corp. of Japan (Abstract only)	04/21/1988	
PB	59	JP	63-119500		Dai Ichi Seiyaku Co Ltd. (English Abstract only)	05/24/1988	No
Examiner Signature	<i>P. Badio</i>				Date Considered	11/15/05	

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		Office <sup>2</sup>	Number <sup>3</sup> (if known)				
BB	60	JP	41 000100	A	Dainippon Pharmaceutical Co., Ltd. (abstract only)	01/07/1966	
	61	JP -	11-209322		Kao Corp (English abstract only)	08/03/1999	No
	62	SU	1240038	A1	A MED ONCOLOGY CENTRE (abstract only)	10/27/1996	
	63	WO	00/07576	A2	ENDORECHERCHE, INC	02/17/2000	
	64	WO	00/10552	A2	Global Vascular Concepts, Inc.	03/02/2000	
	65	WO	00/66095	A2	Sterix Limited	11/09/2000	
	66	WO	00/68246	A1	Research Institute for Medicine and Chemistry Inc.	11/16/2000	
	67	WO	87/02367	A3	The Upjohn Company	04/23/1987	
	68	WO	88/08002	A1	The Upjohn Company	10/20/1988	
	69	WO	93/19746	A1	ORION-YH-TYMA OY	10/14/1993	
	70	WO	98/32763	A1	SRI International	07/30/1998	
	71	WO	99/01142	A1	Hyal Pharmaceutical Corporation	01/14/1999	
BB	72	WO	99/22728	A1	Arch Development Corporation	05/14/1999	

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Examiner Name	Badio, Barbara						
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		Office <sup>3</sup>	Number <sup>4</sup> (if known)				
BP	73	WO	99/33858	A3	SRI International	07/08/1999	
	74	WO	99/33859	A2	SRI International	07/08/1999	
	75	WO	99/35150	A3	Arizona Board of Regents	07/15/1999	
BP	76	WO	99/45018	A1	Imclone Systems Incorporated	09/10/1999	

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BP	77	Author:	Title:		
	Publ:	<u>Research Plus Catalog</u>			
		Vol/iss:	Pages: 50-58	Date: 1993	
	78	Author:	Title: News Article: Hoffman-La Roche Signs \$70 Million Deal with Millenium on Genomics Technology		
		Publ:	<u>Genetic Engineering News</u>		
		Vol/iss:	Pages:	Date: 4/15/1994	
	79	Author:	Title: News Article: Advanced Drug Delivery Systems Peak Interest of Pharmaceutical & Biotech Firms		
		Publ:	<u>Genetic Engineering News</u>		
		Vol/iss:	Pages:	Date: 4/15/1994	
	80	Author:	Title: News Article: Nasal Spray for Treating Bleeding Disorders		
		Publ:	<u>Genetic Engineering News</u>		
		Vol/iss:	Pages:	Date: 4/15/1994	
	81	Author: ABOULWAFA et al.	Title: Synthesis and evaluation for uterotrophic and antiimplantation activities of 2-substituted estradiol derivatives		
		Publ:	<u>Steroids</u>		
		Vol/iss: 57	Pages: 199-204	Date: 04/1992	
	82	Author: ALGIRE, G.H. et al.	Title: Vascular reactions of normal and malignant tumors in vivo. I. Vascular reactions of mice to wounds and to normal and neoplastic transplants		
		Publ:	<u>Journal of the National Cancer Institute</u>		
		Vol/iss: 6	Pages: 73-85	Date: 08/1945	
	83	Author: ALIEV et al.	Title: 54929q Synthesis of cycloalkyl derivatives of dihydric phenols and their ethers		
		Publ:	<u>Chemical Abstracts</u>		
		Vol/iss: 72	Pages: 370	Date: 1970	

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BB	84	Author: ANSTEAD et al.  <u>Publ:</u> <u>Steroids</u>	Title: The Estradiol Pharmacophore: Ligand Structure-Estrogen Receptor Binding Affinity Relationships and a Model for the Receptor Binding Site		
			Vol/iss: 62	Pages: 268-303	Date: 1997
	85	Author: ARNOLDI et al.  <u>Publ:</u> <u>Journal of Agric. Food Chem.</u>	Title: Sweet Isovanillyl Derivatives: Synthesis and Structure-Taste Relationships of Conformationally Restricted Analogs (Abstract only)		
			Vol/iss: 46(10)	Pages: 4002-4010	Date: 1998
BB	86	Author: ATTALLA et al.  <u>Publ:</u> <u>Biochemical and Biophysical Research Communications</u>	Title: 2-Methoxyestradiol-Induced Phosphorylation of Bcl-2: Uncoupling from JNK/SAPK Activation (Abstract only)		
			Vol/iss: 247 (3)	Pages: 616-619	Date: 6/29/1998
	87	Author: AUDIER et al.  <u>Publ:</u> <u>Bulletin De La Societe Chimique De France</u>	Title: Orientation de la fragmentation en spectrometrie de masse par introduction de groupements fonctionnels. VII. - Ethenylenecetals de ceto-2 steroïdes <i>English translation needed</i>		
			Vol/iss: 10	Pages: 3088-3090	Date: 1965
BB	88	Author: BARNES et al.  <u>Publ:</u> <u>Infection and Immunity</u>	Title: Tumor Necrosis Factor Production in Patients with Leprosy		
			Vol/iss: 60 (4)	Pages: 1441-1446	Date: 04/1992
	89	Author: BINDRA et al.  <u>Publ:</u> <u>Journal of Medicinal Chemistry</u>	Title: Studies in Antifertility Agents. 8. Seco Steroids. 2, 5,6-Secoestradiol and Some Related Compounds		
			Vol/iss: 18 (9)	Pages: 921-925	Date: 1975
BB	90	Author: BLICKENSTAFF et al.  <u>Publ:</u> <u>Steroids</u>	Title: Synthesis of Some Analogs of Estradiol		
			Vol/iss: 46 (4,5)	Pages: 889-902	Date: 10/1985

Examiner Signature	P. Davis	Date Considered	11/15/05
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## OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

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BB	91	Author: BOYCE et al.  Publ: Unknown	Title: Some Preliminary Synthetical Studies with 5,6,7,8-Tetra-hydro-8-methylindane -1,5-dione	Vol/Iss:	Pages: 4547-4553 Date: 1960
	92	Author: BRANDI et al.  Publ: Calcif. Tissue Int.	Title: Bone endothelial cells as estrogen targets (Abstract only)	Vol/Iss: 53 (5)	Pages: 312-317 Date: 1993
	93	Author: BREM, H. et al.  Publ: Journal of Neurosurgery	Title: Interstitial chemotherapy with drug polymer implants for the treatment of recurrent gliomas	Vol/Iss: 74	Pages: 441-446 Date: 03/01/91
	94	Author: BURROWS, N.P.  Publ: British Medical Journal	Title: Thalidomide Modifies Disease	Vol/Iss: 307 (6909)	Pages: 939-940 Date: 10/09/93
	95	Author: CAMBIE et al.  Publ: Journal of the Chemical Society	Title: Aromatic Steroids. Part II. Chromium Trioxide Oxidation of Some Oestra-1,3,5(10)-trienes	Vol/Iss: 9	Pages: 1234-1240 Date: 1969
	96	Author: CAMBIE et al.  Publ: J. Chem. Soc.	Title: Aromatic Steroids. Part I. Oxidation Products of 3-Methoxyestra-1,3,5(10)-triene- 17 $\beta$ -yl Acetate	Vol/Iss:	Pages: 2603-2608 Date: 1968
BB	97	Author: COREY et al.  Publ: Tetrahedron Letters	Title: Applications of N,N-Dimethylhydrazones to Synthesis. Use in Efficient, Positionally and Stereochemically Selective C-C Bond Formation; Oxidative Hydrolysis to Carbonyl Compounds	Vol/Iss: 1	Pages: 3-6 Date: 1976

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BB	98	Author: COREY et al.  Publ: <u>Tetrahedron Letters</u>	Title: Facile Conversion of N,N-Dimethylhydrazones to Carbonyl Compounds by Cupric Ion-Catalyzed Hydrolysis	Vol/Iss: 41	Pages: 3678-3668 Date: 1976
	99	Author: CRABBE, P.  Publ: <u>Chem. Ind.</u>	Title: Cotton effect of the styrene chromophore (Abstract only)	Vol/Iss: 27	Pages: 917-918 Date: 1969
	100	Author: D'AMATO, R.J. et al.  Publ: <u>Proceedings of the National Academy of Science USA</u>	Title: Thalidomide is an Inhibitor of Angiogenesis	Vol/Iss: 91	Pages: 4082-4085 Date: 04/01/94
	101	Author: DING et al.  Publ: <u>Endocrinology</u>	Title: Sex Hormone-Binding Globulin Mediates Prostate Androgen Receptor Action via a Novel Signaling Pathway (Abstract only)	Vol/Iss: 139 (1)	Pages: 213-218 Date: 1998
	102	Author: DURANI et al.  Publ: <u>Journal of Steroid Biochemistry</u>	Title: Seco-Oestradiols and Some Non-Steroidal Oestrogens: Structural Correlates of Oestrogenic Action	Vol/Iss: 11	Pages: 67-77 Date: 1979
	103	Author: EDER et al.  Publ: <u>Chem. Ber.</u>	Title: Synthese von Ostradiol (in German - No translation available)  <i>(English Abstract only)</i>	Vol/Iss: 109	Pages: 2948-2953 Date: 1976
BB	104	Author: EL-TOMBARY .  Publ: <u>Arch. Pharm. Pharm. Med. Chem.</u>	Title: Synthesis, Uterotropic, And Antiuterotropic Activities of Some Estradiol Derivatives Containing Thiadiazole, Thiazoline, and Thiazolidinone Moieties	Vol/Iss: 330 (9-10)	Pages: 295-302 Date: 1997

Examiner Signature	Badio	Date Considered	11/18/03
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<sup>1</sup>Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language translation is attached.

<p>Substitute for Form 1449/A/PTO</p> <p><b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> (use as many sheets as necessary)</p>				Complete if Known	
				Application No.	09/644,387
				Filing Date	08/23/2000
				First Named Inventor	Agoston et al.
				Group Art Unit	1617
				Examiner Name	Badio, Barbara
Sheet	10	of	24	Attorney Docket Number	05213-0541 (43170-219662)

**OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS**

Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published			T <sup>2</sup>
BB	105	Author: EMONS et al.  Publ: <u>FOCUS MHL</u>	Title: Modulation der hypophysaren Sekretion von Luteinisierendem Hormon (LH) durch Ostogene	Vol/Iss: 3	Pages: 221-228 Date: 1986
	106	Author: ENYJOJI, K. et al.  Publ: <u>Biochemistry</u>	Title: Effect of Heparin on the Inhibition of Factor Xa by Tissue Factor Pathway Inhibitor: A Segment, Gly <sup>311</sup> -Phe <sup>316</sup> , of the third Kunitz Domain is a Heparin-Binding Site	Vol/Iss: 34 (17)	Pages: 5725-5735 Date: 1995
	107	Author: FANCHENKO et al.  Publ: <u>Byull. Eksp. Biol. Med.</u>	Title: Characteristics of the guinea pig uterus estrogen receptor system (Abstract only)	Vol/Iss: 85 (4)	Pages: 467-470 Date: 1978
	108	Author: FETIZON et al.  Publ: <u>Bull. Soc. Chim. FR.</u>	Title: Synthesis of 2-keto steroids (Abstract only)	Vol/Iss: 8	Pages: 3301-3306 Date: 1968
	109	Author: FEVIG et al.  Publ: <u>Journal of Organic Chemistry</u>	Title: A Short, Stereoselective Route to 16 $\alpha$ (Substituted-alkyl)estradiol Derivatives	Vol/Iss: 52	Pages: 247-251 Date: 1987
	110	Author: FIELD et al.  Publ: <u>Nature</u>	Title: Effect of Thalidomide on the Graft versus Host Reaction	Vol/Iss: 211 (5055)	Pages: 1308-1310 Date: 09/17/66
BB	111	Author: FIESER et al.  Publ: <u>Organic Synthesis Collective Volume 3</u>	Title: N-Methylformanilide	Vol/Iss: 3	Pages: 590-591 Date: 1955

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Sheet	11	of	24	Attorney Docket Number	05213-0541 (43170-219662)

## OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

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BB	112	Author: FLOHE et al.  Publ: <u>Arzneimittelforschung (Germany West)</u>	Title: Studies on the Hypothetical Relationship of Thalidomide-induced Embryopathy and Collagen Biosynthesis	Vol/Iss: 31 (2)	Pages: 315-320 Date: 01/01/81
	113	Author: FOLKMAN et al.  Publ: <u>Science</u>	Title: Angiogenesis Inhibition and Tumor Regression Caused by Heparin or a Heparin Fragment in the Presence of Cortisone	Vol/Iss: 221	Pages: 719-725 Date: 08/19/83
	114	Author: FOLKMAN, J.  Publ: <u>New England Journal of Medicine</u>	Title: Tumor Angiogenesis: Therapeutic Implications	Vol/Iss: 285 (21)	Pages: 1182-1186 Date: 11/18/71
	115	Author: FOLKMAN, J. et al.  Publ: <u>Nature</u>	Title: Induction of Angiogenesis During the Transition from Hyperplasia to Neoplasia	Vol/Iss: 339	Pages: 58-61 Date: 05/04/89
	116	Author: FOLKMAN, J. et al.  Publ: <u>Annals of Surgery</u>	Title: Tumor Behavior in Isolated Perfused Organs in vitro Growth and Metastases of Biopsy Material in Rabbit Thyroid and Canine Intestinal Segment	Vol/Iss: 164(3)	Pages: 491-502 Date: 09/01/66
	117	Author: GADOSY et al.  Publ: <u>Journal of Physical Chemistry</u>	Title: Generation, Characterization, and Deprotonation of Phenol Radical Cations	Vol/Iss: 103	Pages: 8834-8839 Date: 1999
BB	118	Author: GANDHI et al.  Publ: <u>Journal of Indian Chem. Soc.</u>	Title: Mannich Reaction of Estrone  (Abstract Only)	Vol/Iss: 39	Pages: 306-308 Date: 1962

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BB	119	Author: GASLINI et al.  Publ: <u>Journal of Organic Chemistry</u>	Title: Reaction of Eugenol with Synthesis Gas. Synthesis of 5,6,7,8-Tetrahydro -3-methoxy-2-naphthol  <i>(Abstract Only) + document illegible</i>	Vol/Iss: 29 (5)	Pages: 1177-1180 Date: 05/1964
	120	Author: GIAN TONDURY et al.  Publ: <u>Cambridge Philosophical Society</u>	Title: Zur Wirkung Der Sexualhormone Auf Wachstum und Differenzierung (See English Summary Page 55)	Vol/Iss:	Pages: 28-58 Date: 12/17/1955
	121	Author: GIMBRONE, M.A. et al.  Publ: <u>Journal of the National Cancer Institute</u>	Title: Tumor Growth and Neovascularization: An Experimental Model Using the Rabbit Cornea	Vol/Iss: 52(2)	Pages: 413-427 Date: 02/74
	122	Author: GIMBRONE, M.A. et al.  Publ: <u>Journal of Experimental Medicine</u>	Title: Tumor dormancy <i>in vivo</i> by Prevention of Neovascularization	Vol/Iss: 136	Pages: 261-276 Date: 1972
	123	Author: GONZALEZ et al.  Publ: <u>Steroids</u>	Title: Synthesis and Pharmacological Evaluation of 8 $\alpha$ -Estradiol Derivatives	Vol/Iss: 40 (2)	Pages: 171-187 Date: 9/1982
	124	Author: GROSS, J.L. et al.  Publ: <u>Proceedings of the American Association of Cancer Research</u>	Title: Modulation of Solid Tumor Growth <i>in vivo</i> by bFGF (Abstract only)	Vol/Iss: 31	Pages: 79 Date: 03/90
BB	125	Author: GUJJAR et al.  Publ: <u>Annals of Clinical and Laboratory Science</u>	Title: The Effect of Estradiol on Candida albicans Growth	Vol/Iss: 27 (2)	Pages: 151-156 Date: 1997

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BB	126	Author: GUNZLER, V.  Publ: <u>Medical Hypothesis</u>	Title: Thalidomide-A Therapy for the Immunological Consequences of HIV Infection?		
	127	Author: GUPTA et al.  Publ: <u>Indian Journal of Chemistry</u>	Title: Antifertility Agents. XIV. Secosteroids. VII. Synthesis of 2 $\alpha$ and 2 $\beta$ , 6 $\beta$ -dimethyl- 3 $\beta$ -(p-hydroxyphenyl)-trans-bicyclo[4.3.0]nonan-7-ones and some related compounds (Abstract only)	Vol/Iss: 30 (2)	Pages: 105-109 Date: 10/89
	128	Author: GUPTA et al.  Publ: <u>Indian Journal of Chemistry</u>	Title: Studies in Antifertility Agents. Part XVIII. 2 $\alpha$ 6 $\beta$ -Diethyl-3 $\beta$ -(p-hydroxyphenyl)-trans-bicyclo[4.3.0]nonan-7 $\beta$ -ol and 6 $\beta$ -methyl-3 $\beta$ -(p-hydroxyphenyl)-2 $\alpha$ -propyl- trans-bicyclo[4.3.0]nonan-7 $\beta$ -ol (Abstract only)	Vol/Iss: 13 (7)	Pages: 759-760 Date: 1975
	129	Author: GUTIERREZ-RODRIGUEZ et al.  Publ: <u>The Journal of Rheumatology</u>	Title: Treatment of Refractory Rheumatoid Arthritis - The Thalidomide Experience	Vol/Iss: 16 (2)	Pages: 158-163 Date: 02/89
	130	Author: GUTIERREZ-RODRIGUEZ, O.  Publ: <u>Arthritis and Rheumatism</u>	Title: Thalidomide - A Promising New Treatment for Rheumatoid Arthritis	Vol/Iss: 27 (10)	Pages: 1118-1121 Date: 10/84
	131	Author: HAHNEL et al.  Publ: <u>Journal of Steroid Biochemistry</u>	Title: The Specificity of the Estrogen Receptor of Human Uterus	Vol/Iss: 4	Pages: 21-31 Date: 1973
BB	132	Author: HANDLEY et al.  Publ: <u>British Journal of Dermatology</u>	Title: Chronic bullous disease of childhood and ulcerative colitis	Vol/Iss: 127 (40)	Pages: 67-68 Date: 07/01/92

Examiner Signature	Badio	Date Considered	11/15/05
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INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT  
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Sheet 14 of 24

Complete if Known	
Application No.	09/644,387
Filing Date	08/23/2000
First Named Inventor	Agoston et al.
Group Art Unit	1617
Examiner Name	Badio, Barbara

Attorney Docket Number 05213-0541 (43170-219662)

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PB	133	Author: HE et al.  Publ: <u>Bioorganic &amp; Medicinal Chemistry Letters</u>	Title: Novel Cytokine Release Inhibitors. Part II Steroids  Vol/Iss: 8	Pages: 2825-2828	Date: 1998
	134	Author: HEJAZ et al.  Publ: <u>Journal of Medicinal Chemistry</u>	Title: Synthesis and Biological Activity of the Superestrogen (E)-17-Oximino-3-O-sulfamoyl-1,3,5(10)-estratriene: X-ray Crystal Structure of (E)-17-Oximino-3-hydroxy-1,3,5(10)-estratriene  Vol/Iss: 42 (16)	Pages: 3188-3192	Date: 1999
	135	Author: HENRY et al.  Publ: <u>British Journal of Haematology</u>	Title: Thalidomide treatment for chronic graft-versus-host disease  Vol/Iss: 78 (1)	Pages: 23-27	Date: 05/91
	136	Author: HOLKER et al.  Publ: <u>J. Chem. Soc. Perkin Trans.</u>	Title: The Reactions of Estrogens with Benzeneseleninic Anhydride and Hexamethyldisilazane  Vol/Iss: 1	Pages: 1915-1918	Date: 1982
	137	Author: HU, G.  Publ: <u>Proceedings of the National Academy of Sciences, USA</u>	Title: Neomycin Inhibits Angiogenin-induced Angiogenesis (abstract Only)  Vol/Iss: 95 (17)	Pages: 9791-9795	Date: 1998
	138	Author: IKEGAWA et al.  Publ: <u>Biomed. Chromatogr.</u>	Title: Immunoaffinity extraction for liquid chromatographic determination of equulin and its metabolites in plasma (Abstract only)  Vol/Iss: 10 (2)	Pages: 73-77	Date: 1996
PB	139	Author: IMAMURA et al.  Publ: <u>USPATFULL 76,20259 US 3,950,437</u>	Title: Method for Manufacture of Dihydric Phenols (Abstract only)  Vol/Iss: Pages: Date: 04/13/1976		

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11/15/05

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				First Named Inventor	Agoston et al.
				Group Art Unit	1617
				Examiner Name	Badio, Barbara
Sheet	15	of	24	Attorney Docket Number	05213-0541 (43170-219662)
<b>OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS</b>					
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BD	140	Author: INGBER, D. et al.	Title: Synthetic analogues of fumagillin that inhibit angiogenesis and suppress tumor growth		
	Publ: <u>Nature</u>	Vol/Iss: 348	Pages: 555-557	Date: 12/06/90	
	141	Author: IRIARTE et al.	Title: Steroids (XCIV). Synthesis of 2-methyl and 1,2-dimethyl estrogens (Abstract only)		
		Publ: <u>Tetrahedron</u>	Vol/Iss: 3	Pages: 28-36	Date: 1958
	142	Author: JAGGERS et al.	Title: Potent Inhibitory Effects of Steroids in an in vitro Model of Angiogenesis (Abstract only)		
		Publ: <u>Journal of Endocrinology</u>	Vol/Iss: 150 (3)	Pages: 457-464	Date: 1996
	143	Author: JHINGRAN et al.	Title: Studies in Antifertility Agents - Part XLI: Secosteroids-x: Syntheses of Various Stereoisomers of (+)-2,6 $\beta$ -diethyl-7 $\alpha$ -ethynyl-3-(p-hydroxyphenyl)-trans-bicyclo [4.3.0]nonan-7 $\beta$ -ol.		
		Publ: <u>Steroids</u>	Vol/Iss: 42 (6)	Pages: 627-634	Date: 1983
	144	Author: KARWAT	Title: Separation and Recovery of Hydrogen Sulfide from Hydrocarbon Mixture		
		Publ: <u>Caplus DE 1103310</u>	Vol/Iss:	Pages:	Date: 09/02/1959
	145	Author: KATAOKA et al.	Title: An Agent that Increases Tumor Suppressor Transgene Product Coupled with Systemic Transgene Delivery Inhibits Growth of Metastatic Lung Cancer in Vivo (Abstract only)		
		Publ: <u>Cancer Research</u>	Vol/Iss: 58 (21)	Pages: 4761-4765	Date: 11/1998
BD	146	Author: KNIGHTON, D. et al.	Title: Avascular and Vascular Phases of Tumour Growth in the Chick Embryo		
	Publ: <u>British Journal of Cancer</u>	Vol/Iss: 35	Pages: 347-356	Date: 1977	

Examiner Signature	<i>Badio</i>	Date Considered	<i>11/05/05</i>
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BB	147	Author: KOLE et al.  Publ: <u>Journal of Medicinal Chemistry</u>	Title: Studies in Antifertility Agents. II. Secosteroids.5.Synthesis of 9,11-Secoestradiol  Vol/Iss: 18 (7)      Pages: 765-766      Date: 1975		
	148	Author: KOVACS et al.  Publ: <u>Acta Phys.Chem.</u>	Title: Steroids. XXIII. Synthesis of 2- and 4-hydroxy and 2,4-dihydroxy derivatives of estrone and estradiol (Abstract only)  Vol/Iss: 19 (3)      Pages: 287-290      Date: 1973		
	149	Author: LAGUCHEV, S.S.  Publ: <u>Path.-Biol.</u>	Title: Hormonal Regulation of Cell-Divisions in the Mammary Gland  Vol/Iss: 9 (5-6)      Pages: 638-640      Date: 03/1961		
	150	Author: LEWIS, Richard J.  Publ: <u>Hawley's Condensed Chemical Dictionary</u>	Title:  Vol/Iss:      Pages: 577      Date: 01/1993		
	151	Author: LEWIS, Richard J.  Publ: <u>Hawley's Condensed Chemical Dictionary</u>	Title:  Vol/Iss:      Pages: 128-129      Date: 01/1993		
	152	Author: LI, J., et al.  Publ: <u>CAPLUS: Molecular Pharmacology</u>	Title:(DN 103:65176) Catechol Formation of Fluoro- and Bromo-substituted Estradiols by Hamster Liver Microsomes. Evidence for Dehalogenation. (Abstract only)  Vol/Iss: 27 (5)      Pages: 559-565      Date: 1985		
BB	153	Author: LIEN, W. et al.  Publ: <u>Surgery</u>	Title: The blood supply of experimental liver metastases. II. A Microcirculatory study of the normal and tumor vessels of the liver with the use of perfused silicone rubber  Vol/Iss: 68 (2)      Pages: 334-340      Date: 08/1970		

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BB	154	Author: LIMANTSEV et al.  Publ: <u>Akush Jinekol.</u>	Title: Effect of some estrogen structural analogs on the development of the mouse embryo (Abstract only)	Vol/Iss: 6	Pages: 55-56 Date: 1982
	155	Author: LIU et al.  Publ: <u>Tetrahedron Letters</u>	Title: Total Synthesis of (+-) - $\Delta^{9(12)}$ -Capnellene	Vol/Iss: 26 (40)	Pages: 4847-4850 Date: 1985
	156	Author: LOOZEN et al.  Publ: <u>Recl.: J.R. Neth.Chem. Soc.</u>	Title: An approach to the synthesis of 7.β-amino estrogens (Abstract only)	Vol/Iss: 102 (10)	Pages: 433-437 Date: 1983
	157	Author: LOVELY et al.  Publ: <u>Journal of Medicinal Chemistry</u>	Title: 2-(Hydroxyalkyl)estradiols: Synthesis and Biological Evaluation	Vol/Iss: 39	Pages: 1917-1923 Date: 1996
	158	Author: MARO et al.  Publ: <u>Journal of Embryology and Experimental Morphology</u>	Title: Mechanism of Polar Body Formation in the Mouse Oocyte: An Interaction Between the Chromosomes, the Cytoskeleton and the Plasma Membrane	Vol/Iss: 92	Pages: 11-32 Date: 1986
	159	Author: MEZA et al.  Publ: <u>Drug Therapy</u>	Title: Managing the Gastrointestinal Complications of AIDS	Vol/Iss: 23 (11)	Pages: 74-83 Date: 11/1993
BB	160	Author: MICHEL et al.  Publ: <u>Biochem. Pharmacol.</u>	Title: Inhibition of synaptosomal high-affinity uptake of dopamine and serotonin by estrogen agonists and antagonists (Abstract only)	Vol/Iss: 36 (19)	Pages: 3175-3180 Date: 1987

Examiner Signature	<i>Badio</i>	Date Considered	<i>11/15/05</i>
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	161	Author: MOLLENDORFF, W. VON	Title: Wachstumsstörungen durch Geschlechtshormone, nach Untersuchungen an Gewebekulturen <i>English translation needed</i> Publ: Vol/Iss: Pages: 187-202 Date: 06/12/1941		
BB	162	Author: MORISAKI et al.	Title: Steroids. L1. Aromatization reaction of the cross-conjugated dienone system by Zinc 9. (Abstract only) Publ: Chem. Pharm. Bull. Vol/Iss: 14 (8) Pages: 866-872 Date: 1966		
	163	Author: NAAFS et al.	Title: Thalidomide Therapy An Open Trial Publ: International Journal of Dermatology Vol/Iss: 24 (2) Pages: 131-134 Date: 03/1985		
	164	Author: NAMBARA et al.	Title: Microbial transformation products derived from steriods. I. Synthesis of 1,2- and 3-dimethoxy-4-methylestratrienes (Abstract only) Publ: Chem. Pharm. Bull. Vol/Iss: 20 (2) Pages: 336-342 Date: 1972		
	165	Author: NAMBARA et al.	Title: Synthesis of 16β-Oxygenated Catechol Estrogen Methyl Ethers, New and Potential Metabolites Publ: Chemical & Pharmaceutical Bulletin Vol/Iss: 23 (7) Pages: 1613-1616 Date: 07/1975		
	166	Author: NAMBARA, T., et al.	Title: DN 82:43650; Analytical Chemical Studies on Steroids. LXXXIII. Synthesis of Epimeric 2-Hydroxy-16-Cholestrostrong Monomethyl Ethers (Abstract only) Publ: HCAPLUS-Chemical and Pharmaceutical Bulletin Vol/Iss: 22 (10) Pages: 2455-2457 Date: 1974		
BB	167	Author: NEWKOME et al.	Title: Synthesis of Simple Hydrazones of Carbonyl Compounds by an Exchange Reaction Publ: Journal of Organic Chemistry Vol/Iss: 31 Pages: 677-681 Date: 03/1966		

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<p>Substitute for Form 1449/A/PTO</p> <p><b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> (use as many sheets as necessary)</p>				Complete if Known	
				Application No.	09/644,387
				Filing Date	08/23/2000
				First Named Inventor	Agoston et al.
				Group Art Unit	1617
				Examiner Name	Badio, Barbara
Sheet	19	of	24	Attorney Docket Number	05213-0541 (43170-219662)
<b>OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS</b>					
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BB	168	Author: NGUYEN, M. et al.  Publ: <u>Journal of the National Cancer Institute</u>	Title: Elevated Levels of the Angiogenic Peptide Basic Fibroblast Growth Factor in Urine of Bladder Cancer Patients		
		Vol/Iss: 85 (3)	Pages: 241-242	Date: 02/03/93	
	169	Author: NUMAZAWA et al.  Publ: <u>Steroids</u>	Title: Novel and Regiospecific Synthesis of 2-Amino Estrogens via Zincke Nitration		
			Vol/Iss: 41 (5)	Pages: 675-682	Date: 1983
	170	Author: OMAR et al.  Publ: <u>European Journal of Medicinal Chemistry</u>	Title: Synthesis, binding affinities and uterotrophic activity of some 2-substituted estradiol and ring-A-fused pyrone derivatives		
			Vol/Iss: 29	Pages: 25-32	Date: 1994
	171	Author: PERT et al.  Publ: <u>Australian Journal of Chemistry</u>	Title: Preparations of 2,4-disubstituted estradiols (Abstract only)		
			Vol/Iss: 42 (3)	Pages: 421-432	Date: 1989
	172	Author: PETERS et al.  Publ: <u>Journal of Medicinal Chemistry</u>	Title: 17-Desoxy Estrogen Analogs		
			Vol/Iss: 32 (7)	Pages: 1642-1652	Date: 1989
	173	Author: PFEIFFER et al.  Publ: <u>Journal of Endocrinology</u>	Title: Are catechol estrogens obligatory mediators of estrogen action in the central nervous system? I. Characterization of pharmacological probes with different receptor binding affinities and catechol estrogen formation rates (Abstract only)		
			Vol/Iss: 110 (3)	Pages: 489-497	Date: 1986
BB	174	Author: PLUM et al.  Publ: <u>Proceedings of the American Association for Cancer Research Annual</u>	Title: Vaccination with Peptide to the Heparin Binding Domain of bFGF Conjugated to Liposomes Inhibits bFGF Induced Neovascularization (Abstract only)		
		Vol/Iss: 39	Pages: 8	Date: 03/1998	

Examiner Signature	<i>Badio</i>	Date Considered	<i>11/15/05</i>
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				Filing Date	08/23/2000
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				Examiner Name	Badio, Barbara
Sheet	20	of	24	Attorney Docket Number	05213-0541 (43170-219662)

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BB	175	Author: POWELL et al.  Publ: <u>British Journal of Dermatology</u>	Title: Investigation and Treatment of Orogenital Ulceration; studies on a Possible Mode of Action of Thalidomide		
	176	Author: ROMANELLI et al.  Publ: <u>Organic Synthesis</u>	Title: Ethyl- <i>p</i> -Dimethylaminophenylacetate  Vol/Iss: 113 Supp. 28	Pages: 141-144	Date: 07/1985
	177	Author: SAKAKIBARA, KYOICHI  Publ: <u>Chemical Abstracts</u>	Title: 2-Hydroxy-1,3,5(10)-estratriene derivatives (Abstract only) (Identifier: XP-002186126)  Vol/Iss: 60(1)	Pages: 552	Date: 10/24/1973
	178	Author: SATO et al.  Publ: <u>Horm. Carcinog. II. Proceedings Int. Symp., 2nd (1996). Meeting Date 1994</u>	Title: Natural estrogens induce modulation of microtubules in Chinese hamster V79 cells in culture (Abstract only)  Vol/Iss:	Pages: 454-457	Date: 1996
	179	Author: SEAVER, Sally  Publ: <u>Genetic Engineering News</u>	Title: Monoclonal Antibodies in Industry: More Difficult than Originally Thought  Vol/Iss: 14	Pages: 10 and 21	Date: 08/1994
	180	Author: SEEGERS et al.  Publ: <u>Joint MCI-1st Symposium, Third 1st International Symposium, Biology and Therapy of Breast Cancer</u>	Title: Cyclic-AMP and Cyclic-GMP Production in MCF-7 Cells Exposed to Estradiol-17 Beta, Catecholestrogens and Methoxy-Estrogens in MCF-7 Cells (Meeting Abstract only)  Vol/Iss:	Pages:	Date: 09/25/89
BB	181	Author: SEEGERS et al.  Publ: <u>Journal of Steroid Biochemistry and Molecular Biology</u>	Title: The Mammalian Metabolite, 2-methoxyestradiol, Affects P53 Levels and Apoptosis Induction in Transformed Cells but Not in Normal Cells (Abstract only)  Vol/Iss: 62 (4)	Pages: 253-267	Date: 07/1997

Examiner Signature	Badio	Date Considered	11/15/05
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				Group Art Unit	1617
				Examiner Name	Badio, Barbara
Sheet	21	of	24	Attorney Docket Number	05213-0541 (43170-219662)

## OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

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BP	182	Author: SHAH et al.  Publ: <u>Journal of Medicinal Chemistry</u>	Title: (+/-)-N-alkylamino)benzazepine Analogs: Novel Dopamine D1 Receptor Antagonists (Abstract only)	Vol/Iss: 38 (21)	Pages: 4284-4293	Date: 10/13/95
	183	Author: SHISHKINA et al.  Publ: <u>Khim.-Farm. Zh.</u>	Title: Synthesis and properties of condensed heterocyclic derivatives of estra-4, 9-dien-17.beta.-ol-3-one (Abstract only)	Vol/Iss: 8 (1)	Pages: 7-11	Date: 1974
	184	Author: SIDKY et al.  Publ: <u>Cancer Research</u>	Title: Inhibition of Angiogenesis by Interferons: Effects on Tumor- and Lymphocyte-induced Vascular Responses	Vol/Iss: 47	Pages: 5155-5161	Date: 10/01/87
	185	Author: SIRACUSA et al.  Publ: <u>Journal of Embryology and Experimental Morphology</u>	Title: The Effect of Microtubule- and Microfilament-disrupting Drugs on Preimplantation Mouse Embryos (abstract Only)	Vol/Iss: 60	Pages: 71-82	Date: 12/1980
	186	Author: SOKER et al.  Publ: <u>Cell</u>	Title: Neuropilin-1 is Expressed by Endothelial and Tumor Cells as an Isoform-Specific Receptor for Vascular Endothelial Growth Factor	Vol/Iss: 92	Pages: 735-745	Date: 03/20/1998
	187	Author: SPYRIOUNIS et al.  Publ: <u>Arch. Pharm.</u>	Title: Copper (II) complex of an estradiol derivative with potent antiinflammatory properties (Abstract only)	Vol/Iss: 324 (9)	Pages: 533-536	Date: 1991
BP	188	Author: SRIVASTAVA, A. et al.  Publ: <u>American Journal of Pathology</u>	Title: The Prognostic Significance of Tumor Vascularity in Intermediate-Thickness (0.76-4.0 mm Thick) Skin Melanoma	Vol/Iss: 133 (2)	Pages: 419-424	Date: 11/1988

Examiner Signature	<i>Badio</i>	Date Considered	<i>11/18/05</i>
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Sheet	22	of	24	Attorney Docket Number	05213-0541 (43170-219662)

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BB	189	Author: STAPLES et al.  Publ: <u>Steroids</u>	Title: Structural Requirements for Steroid Inhibition of Sheep Lymphocyte Mitogenesis in vitro	Vol/Iss: 44 (5)	Pages: 419-433 Date: 11/1984
	190	Author: STARKOV et al.  Publ: <u>Zhurnal Prikladnoi Khimii</u>	Title: Mono- and Dialkylation of Guaiacol by Olefins on KU-2 Cation Exchanger (Abstract only)	Vol/Iss: 41 (3)	Pages: 688-690 Date: 1968
	191	Author: TAYLOR, S. et al.  Publ: <u>Nature</u>	Title: Protamine is an Inhibitor of Angiogenesis	Vol/Iss: 297	Pages: 307-312 Date: 05/27/82
	192	Author: TREMBLAY et al.  Publ: <u>Synthetic Communications</u>	Title: A Convenient Synthetic Method for Alpha-Alkylation of Steroidal 17-Ketone: Preparation of 16 $\beta$ -(THPO-Heptyl)-Estradiol	Vol/Iss: 25 (16)	Pages: 2483-2495 Date: 1995
	193	Author: TREMBLAY et al.  Publ: <u>Bioorganic &amp; Medicinal Chemistry</u>	Title: Synthesis of 16-(Bromoalkyl)-Estradiols Having Inhibitory Effect on Human Placental Estradiol 17 $\beta$ -Hydroxysteroid Dehydrogenase (17 $\beta$ HSD Type 1)	Vol/Iss: 3 (5)	Pages: 505-523 Date: 1995
	194	Author: VICENTE et al.  Publ: <u>Archives of Internal Medicine</u>	Title: In Vitro Activity of Thalidomide Against Mycobacterium avium Complex	Vol/Iss: 153 (4)	Pages: 534 Date: 02/22/93
BD	195	Author: WANG et al.  Publ: <u>Shengwu Huaxue Zazhi</u>	Title: Photoaffinity Labeling of Human Placental Estradiol 17 $\beta$ -dehydrogenase with 2-And 4-azidoestrone, 2- and 4-azidoestradiol (abstract Only)	Vol/Iss: 8 (6)	Pages: 715-718 Date: 1992

Examiner Signature	<i>Badio</i>	Date Considered	11/15/03
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INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT  
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Sheet	23	of	24	Attorney Docket Number	05213-0541 (43170-219662)
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BP	196	Author: WEIDNER, N. et al.  Publ: <u>Journal of the National Cancer Institute</u>	Title: Tumor angiogenesis: A New Significant and Independent Prognostic Indicator in Early-Stage Breast Carcinoma  Vol/Iss: 84	Pages: 1875-1887	Date: 12/16/92
	197	Author: WEIDNER, N. et al.  Publ: <u>American Journal of Pathology</u>	Title: Tumor Angiogenesis Correlates with Metastasis in Invasive Prostate Carcinoma  Vol/Iss: 143 (2)	Pages: 401-409	Date: 08/1993
	198	Author: WEIDNER, N. et al.  Publ: <u>New England Journal of Medicine</u>	Title: Tumor Angiogenesis and Metastasis-Correlation in Invasive Breast Carcinoma  Vol/Iss: 324 (1)	Pages: 1-8	Date: 01/03/91
	199	Author: WELSCH et al.  Publ: <u>Experientia</u>	Title: Staphylostatic Activity of Some New Diphenols, Naphthols, and Chalcones (Abstract only)  Vol/Iss: 11	Pages: 350-351	Date: 1955
	200	Author: WHITE et al.  Publ: <u>The New England Journal of Medicine</u>	Title: Treatment of Pulmonary Hemangiomatosis with Recombinant Interferon Alfa-2a  Vol/Iss: 32 (18)	Pages: 1197-1200	Date: 05/04/89
	201	Author: WIESE et al.  Publ: <u>Journal of Medicinal Chemistry</u>	Title: Induction of the Estrogen Specific Mitogenic Response of MCF-7 Cells by Selected Analogues of Estradiol-17 $\beta$ : A 3D QSAR Study  Vol/Iss: 40	Pages: 3659-3669	Date: 1997
BP	202	Author: WURTZ et al.  Publ: <u>Journal of Medicinal Chemistry</u>	Title: Three-Dimensional Models of Estrogen Receptor Ligand Binding Domain Complexes Based on Related Crystal Structures and Mutational and Structure-Activity Relationship Data  Vol/Iss: 41	Pages: 1803-1814	Date: 1998

Examiner Signature	<i>Baroio</i>	Date Considered	<i>11/10/03</i>
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BB	203	<p>Author: YASUDA et al.</p> <p>Publ: Anat. Embryol. (Berl.)</p> <p>Title: Accelerated differentiation in seminiferous tubules of fetal mice prenatally exposed to ethinyl estradiol (Abstract only)</p> <p>Vol/Iss: 174 (3)</p> <p>Pages: 289-299</p> <p>Date: 1986</p>	

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